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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/510,332	02/22/00	ZUKER C	2307E-098010

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EXAMINER	
LANDSMAN, R	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No. 09/510,332	Applicant(s) ZUKER ET AL.	
	Examiner Robert Landsman	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-93* is/are pending in the application.

4a) Of the above claim(s) *2-18 and 46-93* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 20-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. Formal Matters

A. The Raw Sequence Listing, filed 1/31/01, has been entered into the record.

B. Claims 1-93 were pending in the instant application and were subject to restriction. Applicants elected claims 1-45, with traverse and argue that the four groups set forth by the Examiner in the restriction requirement all stem from a common concept and theory and are, thus, related. Applicants' arguments have been considered, but are not deemed persuasive. Applicants have elected the claims drawn to a method using the protein of SEQ ID NO:1. Groups II-IV do not include SEQ ID NO:1 and, therefore, since each of the polynucleotides and polypeptides disclosed in the remaining groups are independent and distinct, they would require separate searches.

Claims 1-45 were to be examined insofar as they read on SEQ ID NO:1. However, claims 2-18 will not be examined as they are drawn to a non-elected SEQ ID NO. Therefore, claims 1 and 19-45 will be examined in the present application. This restriction is deemed proper and is made FINAL.

2. Claim Objections

A. Claims 1-45 are objected to since they recite SEQ ID NOs which have not been elected in the present application. It is suggested that Applicants amend the claims to remove reference to any SEQ ID NOs which have not been examined (i.e. all but SEQ ID NO:1).

3. Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

A. Claims 1 and 19-45 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific and substantial asserted utility or a well established utility. These claims are drawn to an invention with no apparent or disclosed patentable utility. This rejection is not in conflict with the current utility guidelines. The instant application has provided a description of a partially isolated protein. However, the instant application does not disclose the biological role of this protein or its significance. The application states that the receptor (SEQ ID NO:1) of the present invention has been characterized as a taste receptor based only on homology.

It is clear from the instant specification that the claimed receptor is termed an "orphan receptor" in the art. There is little doubt that, after complete characterization, this protein will probably be found to have a patentable utility. This further characterization, however, is part of the act of invention and, until it has been undertaken, Applicants' claimed invention is incomplete.

The instant situation is directly analogous to that of which was addressed in Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. 101, which required that an invention must have either an immediate obvious or fully disclosed "real-world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility," "[u]nless and until a process is refined and developed to this point - where specific benefit exists in currently available form – there is insufficient justification for permitting an applicant to engross what may prove to be a broad field," and "a patent is not a hunting license," "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a protein which has a yet undetermined function or biological significance. There is no actual and specific significance which can be attributed to said protein identified in the specification. For this reason, the instant invention is incomplete. In the absence of a knowledge of the natural ligands or biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of substances which bind to and/or mediate activity of the said receptor is clearly to use it as the object of further research which has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real-world" use for said protein then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful.

Therefore, because the receptor of SEQ ID NO:1 is not supported by a specific and substantial asserted utility or a well established utility, then the methods for identifying compounds which modulate the receptor of SEQ ID NO:1 is also not supported by a specific and substantial asserted utility or a well established utility.

4. Claim Rejections - 35 USC § 112, first paragraph – lack of enablement

A. The specification is objected to and claims 1 and 19-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to use the instant invention. Specifically, since the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

B. Furthermore, even if Applicants *were* able to show utility, claims 1 and 19-45 would be rejected under 35 USC 112, first paragraph the breadth of the claims is extensive with regard to claiming all polypeptides which have "**60% amino acid sequence identity**" to SEQ ID NO:1 as well as all

"**activities**" of these receptors. The protein would have one or more amino acid substitutions, deletions, insertions and/or additions to the protein of SEQ ID NO:1. Applicants provide no guidance or working examples of proteins which differ from that of SEQ ID NO:1, nor of all possible activities of these receptors. Furthermore, it is not predictable to one of ordinary skill in the art how to make a functional taste receptor other than that claimed as SEQ ID NO:1, nor what these activities would be. Therefore, even if the protein of the invention was shown to have utility, the extensive breadth of the claims regarding all proteins which are at least 60% identical to SEQ ID NO:1, along with the lack of guidance and working examples of how to make these proteins, as well as the lack of predictability to one of ordinary skill in the art how to make a functional taste receptor which is at least 60% identical to SEQ ID NO:1, would lead the Examiner to hold that undue experimentation is necessary to practice the invention as claimed.

5. Claim Rejections - 35 USC § 112, first paragraph – lack of written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 20-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 20 and 39 are genus claims. The term "**60% amino acid sequence identity**" can mean a protein having one or more amino acid insertions, substitution, or deletions to SEQ ID NO:1. The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Furthermore, claims 21 and 41 recite a method of identifying modulators of a protein which is

60% identical to SEQ ID NO:1 as long as it has a G protein-coupled receptor "**activity**". However, Applicants provide no written description of what this activity is. These activities could include protein-protein interactions, cell growth, or simply an interaction with water, as long as the protein is at least 60% identical to SEQ ID NO:1. One skilled in the art cannot reasonably visualize or predict all activities of all proteins which have a G protein-coupled receptor activity since the specification does not describe these assays. In addition, claims 24 and 44 are genus claims since Applicants have not described which "**extracellular domain**" or "**transmembrane region**" of the receptor is involved in transducing a function.

Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although these types of changes are routinely done in the art, the specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:1 alone is insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Claims 21-38 and 40-45 are rejected since they depend from rejected base claims.

6. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 20-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 1 and 20-36 and 38-45 are confusing since it is not clear what the term "**taste signaling**" refers to or how one knows when they have modulated "taste signaling." It is not understood how simply determining a "functional effect" of a compound as recited, for example, in claim 21, can demonstrate that a compound has somehow affected taste. Claim 37 is objected to since it depends from rejected base claims.

B. Claims 20-45 are confusing since it is not clear what is meant by "**functional effect.**" Claims 22-24 and 44, for example, recite that the function is a "**chemical**" or "**physical**" effect. These terms, too, are unclear. Similarly, claims 24 and 44 recite that the functional effect can be determined by measuring the binding of various compounds to the polypeptide. However, the artisan would readily admit that binding assays are not necessarily indicative of a functional effect. For example, antagonists can bind to receptors and, by definition, do not produce a functional effect.

C. Claim 21 is confusing since the metes and bounds of the term "**activity**" are not known. For example, "activity" could constitute transportation throughout a cell, alteration of tertiary structure due to changes in pH, ligand binding, or modulation of second messenger effect, etc.

7. Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

A. Claims 20-33, 39, 41, 44 and 45 rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. in view of Sambrook et al. and further in view of Ogura et al. (J. Neurosci. 17:3580-3587, 1997). The claims teach a method of identifying compounds that modulate signaling in taste cells by contacting a G protein-coupled receptor which is at least 60% identical to SEQ ID NO:1. The claims also teach a method of identifying chemical and physical effects in a cell. Measurements include measuring GTP binding, electrical activity, IP3 and calcium levels.

Adams et al. teach a DNA molecule which encodes a human protein which is 68% identical to that of SEQ ID NO:1. Adams et al. do not teach the insertion of this DNA clone into a vector and the introduction of this vector into a host cell. However, Sambrook et al. do teach the insertion of DNA into an expression vector and the transfection of a host cell (see entire document, especially pages 14.3 – 14.10).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the invention of Sambrook et al. by substituting a DNA molecule in the polycloning region of the vector with the polynucleotide (DNA) of Adams et al. for the purpose of transfecting a host cell.

Neither Adams et al. or Sambrook et al. teach a method of identifying chemical, physical effects and binding to the polypeptide which is expressed in a cell. Measurements include measuring electrical activity and calcium levels. However, Ogura et al. do teach the screening of a taste receptor using various compounds including denatonium (Figure 2). IP3, calcium levels, which were measured using FURA-2,

and electrophysiological measurements were performed (Figures 2 – Figure 7). These effects are considered both chemical and physical. Since the G protein-coupled taste receptors were expressed on the cell surface and, therefore, have exposed extracellular ligand binding domains, the measurement of an intracellular effect, such as calcium levels, IP3 formation, or electrophysiological effects would be a method of determining a functional effect of the test compound on these extracellular or transmembrane regions since this binding would cause the conformational changes necessary to produce these intracellular effects.

One of ordinary skill in the art would have been motivated to substitute the DNA of Adams et al. into the vector of Sambrook et al. in order to express the protein in a host cell to perform ligand binding studies, as well as functional assays, as taught by those performed on the taste receptors as taught by Ogura et al. In addition, it would have been obvious to one of ordinary skill in the art to have used various types of host cells in which to transfect the DNA of Adams et al., including HEK-293 cells since these cells are one of the most frequently used cells for transfection studies of mammalian DNA. Furthermore, it is well known that G protein-coupled receptors, as the name implies, which encompass taste receptors, couple to G proteins. Therefore, the measurement of radiolabeled GTP, which binds to G proteins upon activation and is the first step in activation of a G protein-coupled receptor, including taste receptors, would be an obvious way to observe the functional effects of a compound on the test receptor. There would have been a reasonable expectation of success for a person of ordinary skill in the art to make and use this invention since these techniques are widely used in the art and are highly successful. The present invention, therefore, is *prima facia* obvious over the above references in the absence of evidence to the contrary.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
April 09, 2001

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